

II. AMENDMENTS

In the Specification:

Please amend paragraphs 116 and 202 as follows:

116 Where desired, sequences from novel heterodimeric receptors can be employed in constructing the subject Abus. In such situation, the identification of a candidate heterodimerization sequences in a given receptor pair can be determined by any generic or biochemical assays without undue experimentation. Additionally, computer modeling and searching technologies further facilitates detection of heterodimerization sequences based on sequence homologies of common domains appeared in related and unrelated genes. Non-limiting examples of programs that allow homology searches are Blast (<http://www.ncbi.nlm.nih.gov/BLAST/>), Fasta (Genetics Computing Group package, Madison, Wisconsin), DNA Star, Clustlaw, TOFFEE, COBLATH, Genthreader, and MegAlign. Any sequence databases that contains DNA sequences corresponding to a target receptor or a segment thereof can be used for sequence analysis. Commonly employed databases include but are not limited to GenBank, EMBL, DDBJ, PDB, SWISS-PROT, EST, STS, GSS, and HTGS.

202 We have modified the carboxyl terminus of GR1 and GR2 domains by adding a flexon "SerArgGlyGlyGlyGly" (amino acid residues 1 through 6 in SEQ ID NOS. 2 or 4) to the amino-terminus of GR1 and GR2 domains to provide additional flexibility to the V regions. To further stabilize ccFv, we have introduced a pair of cysteine residues by adding "ValGlyGlyCys" spacer at the C-termini of the coiled coil. The GR1 and GR2 domains are fused to the carboxyl terminus of VH and VL fragment respectively. The VH-GR1 and VL-GR2 fusions were expressed in *E. coli* and displayed by phage. As shown in Figures 10-11, functional heterodimeric ccFv Abus stabilized by the parallel coiled-coil helix were generated. Since the coiled-coil heterodimerization sequences are about half the size of CH1 and CL domains, the ccFv (approximately 35 kDa) is smaller than the conventional Fab fragments (approximately 50 kDa). Because of the small size,

C2
4

the ccFvs and its derivatives are potentially more useful for clinical applications such as tumor and tissue penetration. More efficient expression and display of ccFv is expected. Furthermore, the specific assembly of VH and VL regions due to the pairwise affinity of the unique heterodimerization sequences makes the construction of a robust, vast diverse repertoire of Abs more feasible.
